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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/811,359	03/16/2001	Taeyoung Yoon	49662 [72021]	7721

21874 7590 08/22/2007

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BOSTON, MA 02205

EXAMINER	
MURRAY, JEFFREY H	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
08/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/811,359	YOON ET AL.	
	Examiner	Art Unit	
	Jeffrey H. Murray	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-22,30,35,39-64,67 and 69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-22,30,35,39-64,67 and 69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *STN prior art information*.

DETAILED ACTION

Applicant's amendment of May 30, 2007 has been fully considered. This action is in response to a response to a non-final action filed on August 10, 2006. Currently, Claims 2, 23-29, 31-34, 36-38, 65, 66 and 68 are cancelled and Claims 1, 3-22, 30, 35, 39-64, 67 and 69 are considered herein.

1. It is acknowledged that applicants have amended Claim 30 to avoid the 112, 2nd rejection.

2. It is acknowledged that applicants have amended Claim 3, 9, 14, 17, and 22 to avoid the 102(b) rejection.

New Grounds for Rejection

Claim Rejections - 35 USC § 112, 1st

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 3-22, 30, 35, and 69 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds or compositions with a pyrimidine that contains a substituted phenyl in the 2-position (Ar), an alkoxy group in the 4-position, and a dialkylamino group in the 5-position (R^2), does not reasonably provide enablement for all of the compounds

and residue groups listed within the Claims, including most of the functional groups found in R^1, R^2, and R^3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

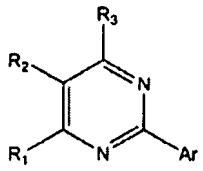
The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation. (*United States v. Teletronics* Inc., 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based on a single factor, but rather a conclusion reached by weighing many factors (See *Ex parte Forman* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). These factors include the following:

1) *Amount of guidance provided by Applicant.* While the Applicant has demonstrated within the application how to make 2-substituted phenyl-4-alkoxy-5-dialkylamino pyrimidines, the generic Claims 1, 3, 9, and 15 are massive, and no reference is made as to how to synthesize any compounds that contain all the various and multiple R groups that are listed within these Claims other than the groups aforementioned. Page 33-34 of the specification provides three different Schemes for synthesizing all of the various final compounds. Applicants point to a 1983 Journal of Organic Chemistry paper to synthesize the starting materials of Compound IV. However this journal article does not provide the details on how to synthesize all of the millions of starting materials needed to make each and every compound claimed throughout this application.

2) *Unpredictability in the art.* It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. (USPQ 18, 24 (CCPA 1970). See *In re Fisher*, 427 F.2d 833, 839, 166.

Page 33-34 of the specification provides three different Schemes for synthesizing all of the various final compounds. In each Scheme, a reduction step (as well as an additional reductive amination step in two of the Schemes) takes place with the R^1 and R^3 groups present. Yet the possible substitutents listed for R^1 and R^3 include cyano, nitro, substituted or unsubstituted alkenes and alkynes, alkylsulfinyl and alkylsulfonyl groups and carboxamides. In one particular instance (that of reducing a nitro group), the exact group being reduced is also listed as an R group which is may be present during that reduction. This is clearly not possible. For example, a sodium triacetoxy-borohydride reaction can cause the hydroboration of alkenes, (Gribble, et. al., p. 9) while the palladium on carbon reduction is notorious for reducing the double and triple bonds of alkenes, alkynes, and nitriles as well as potentially removing a halogen from an aromatic or pyrimidine ring. (King, et. al. pp. 1-3, 7).
The literature and arguments presented here clearly show that a vast majority of the potential R groups cannot exist under the present application's reaction conditions.

3) *Breadth of the claims.* The scope of the claims involve all of the millions of compounds of general formula (I):



whereby Ar, R^1, R^2, and R^3 are defined within the specification. Thus, the scope of claims is incredibly broad.

4) *Nature of the invention.* The nature of the invention relates generally to novel substituted 2-arylpyrimidine compounds that bind with high selectivity and/or high affinity to CRF1 receptors.

5) *Level of skill in the art.* The artisan using Applicants invention would be a chemist with a Ph.D. degree, and having several years of laboratory bench experience.

MPEP §2164.01 (a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here that Applicant is not enabled for making most of the compounds or compositions mentioned in the current application.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Christensen, et. al., Journal of Organic Chemistry, (1971), 36(17), pp.2462-6. The currently claimed compounds read on the compound of the prior art. Whereby the structure contains a pyrimidine with a phenyl in the 2-position, a methoxy group in the 4- and 6-positions, and a nitro group in the 5-position. See CA reference # 29939-35-3.

3. Claim 3, 5, 15, 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Kameko, et. al., JP 10237447, which was published on September 8, 1998. The currently claimed compounds read on the compounds of the prior art. Whereby the structure contains a pyrimidine with a para-hexylphenyl in the 2-position, a hydrogen in the 4- and 6-positions, and an octoxy group in the 5-position. See CA reference # 155430-65-2.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

20. Claims 1, 3-22, 30, 35, 39-64 and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kleemann et. al. in view of Hoefle et. al.

The current application recites a variety of specific novel substituted 2-arylpyrimidine compounds that bind with high selectivity and/or high affinity to CRF1 receptors. These compounds all contain a substituted phenyl in the 2-position (Ar), an alkoxy group in the 4-position, and a dialkylamino group in the 5-position (R^2).

The patent reference Kleemann et. al. teaches a group of compounds which are similar in scope to the current application. Within Kleemann et. al., (See Formula I, col.1) the same core structure is present which teach these compounds as being used for a similar purpose as the proposed application. That is, the 2-arylpyrimidine compounds were synthesized and tested to be used as an herbicidal agent.

Kleemann et. al. has an identical core structure to the current patent application with one major difference. Kleemann et. al. teaches an aryloxy group in the 4-position, not the alkoxy group taught by the present application.

The patent reference, Hoefle et. al., teaches a group of compounds which are similar in scope to the current application. Within Hoefle et. al. (col. 2), a similar core structure is present which teaches these compounds with one difference from the current application. The patent reference compounds are missing a substituted phenyl ring in the 2-position. That is, the reference compounds contain a pyrimidine with a alkoxy group in the 4- and 6-positions, and an amino group in the 5-position, both of which would fall under the current applicants' Claims. However the compounds contain a hydrogen in the 2-position in place of a substituted phenyl ring.

Relating this information to the Kleemann et. al. patent, it would have been obvious for a person of ordinary skill in the art to try replacing the aryloxy group in the 4-position of the Kleemann patent with an alkyloxy group such as the one discussed in the Hoefle patent at the same position on the pyrimidine ring in an attempt to obtain a compound or composition which possesses enhanced activity and to afford a positive benefit from the replacement.

Conclusion

Claims 1, 3-22, 30, 35, 39-64 and 69 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey H. Murray whose telephone number is (571) 272-9023. The examiner can normally be reached on Mon.-Thurs. 7:30-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

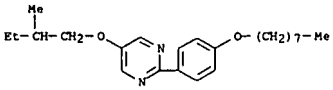
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JHM

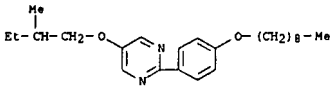
JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

To Be Mailed

L5 ANSWER 19 OF 565 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Pyrimidine, 5-(2-methylbutoxy)-2-[4-(octyloxy)phenyl]- (9CI) (CA INDEX NAME)



RN 218770-20-8 CAPLUS
CN Pyrimidine, 5-(2-methylbutoxy)-2-[4-(nonyloxy)phenyl]- (9CI) (CA INDEX NAME)



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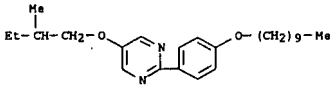
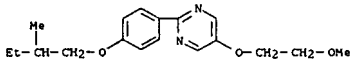
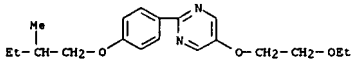
CN Pyrimidine, 2-[4-(decyloxy)phenyl]-5-(2-methylbutoxy)- (9CI) (CA INDEX NAME)



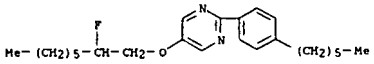
RN 218770-22-0 CAPLUS
CN Pyrimidine, 5-(2-methoxyethoxy)-2-[4-(2-methylbutoxy)phenyl]- (9CI) (CA INDEX NAME)



RN 218770-23-1 CAPLUS
CN Pyrimidine, 5-(2-ethoxyethoxy)-2-[4-(2-methylbutoxy)phenyl]- (9CI) (CA INDEX NAME)



L5 ANSWER 20 OF 565 CAPLUS COPYRIGHT 2007 ACS on STN
IT 155430-65-2 155430-66-3 155430-67-4
155430-68-5
RL: DEV (Device component use); USES (Uses)
(ferroelec. liquid crystal display device with large temperature-dependency of
self-polarization)
RN 155430-65-2 CAPLUS
CN Pyrimidine, 5-[(2-fluorooctyl)oxy]-2-(4-hexylphenyl)- (9CI) (CA INDEX NAME)



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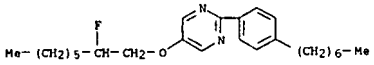
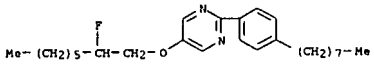


RN 155430-67-4 CAPLUS
CN Pyrimidine, 5-[(2-fluorooctyl)oxy]-2-(4-octylphenyl)- (9CI) (CA INDEX NAME)



RN 155430-68-5 CAPLUS
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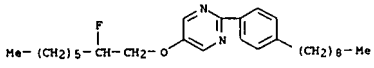

L5 ANSWER 19 OF 565 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 218770-24-2 CAPLUS
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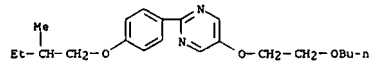

RN 218770-25-3 CAPLUS
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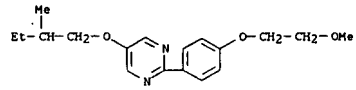

RN 218770-26-4 CAPLUS
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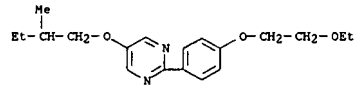
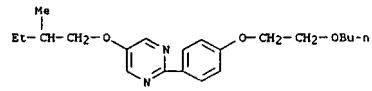


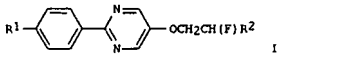
RN 218770-27-5 CAPLUS
CN Pyrimidine, 2-[4-(2-butoxyethoxy)phenyl]-5-(2-methylbutoxy)- (9CI) (CA INDEX NAME)



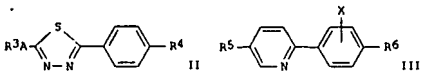
L5 ANSWER 20 OF 565 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:586487 CAPLUS
DOCUMENT NUMBER: 129:268250
TITLE: Ferroelectric liquid-crystal composition, ferroelectric liquid-crystal device, and its driving method
INVENTOR(S): Kaneko, Takeshi; Koden, Mitsuhiro; Okabe, Eiji; Shunto, Tatsuji; Saito, Shinichi; Saito, Hideo
PATENT ASSIGNEE(S): Sharp Corp., Japan; Chisso Corp.
SOURCE: Jpn. Kokai Tokkyo Koho, 17 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10237447	A	19980908	JP 1997-46528	19970228
PRIORITY APPLN. INFO.:			JP 1997-46528	19970228
OTHER SOURCE(S):	MARPAT 129:268250			

GI



I



II III

AB The composition contains an aromatic compound I (R1 = C4-16 alkyl; R2 = C2-12 alkyl), II (R3, 4 = C1-15 alkyl, alkoxy; A = Ph, C6H8, direct bond), and III (R5, 6 = C1-18 alkyl, alkoxy; X = H, F). The device contains the composition Driving method of the device is also claimed. The composition shows large temperature-dependency of self-polarization, so that the device shows small temperature-dependency of response speed and wide temperature margin.

To Be Mailed

L24 ANSWER 22 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1971:510265 CAPLUS <<LOGINID::20070815>>
DOCUMENT NUMBER: 75:110265
TITLE: Reaction of 4,6-dimethoxy-5-nitropyrimidine with methylhydrazine. Formation of 4-hydrazine-6-hydroxypyrimidine
AUTHOR(S): Christensen, Bert E.; Stahl, Quade; Lehmkuhl, Frank
CORPORATE SOURCE: Dep. Chem., Oregon State Univ., Corvallis, OR, USA
SOURCE: Journal of Organic Chemistry (1971), 36(17), 2462-6
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 75:110265

AB Reaction of 4,6-dimethoxy-5-nitropyrimidine (I) with MeNHNH2 in refluxing pyridine or BuOH involves methylation of the solvent by I and the nucleophilic substitution and demethylation of the methylhydrazino substituent in the 5 position to yield 4-hydrazino-6-hydroxypyrimidine. The first step in this sequence of reactions involves the methylation of the solvent, followed by nucleophilic substitution of methylhydrazine in the 4 position, migration of its Me substituent to form C to O bond with the adjacent nitro substituent, and eventual elimination of Me nitrite from the 5 position as one of the reaction products. 4,6-Dimethoxy-5-nitropyrimidine reacts with pyridine (in the absence of MeNHNH2) to yield an insol. methylpyridium salt which is not a precursor of 4-hydrazino-6-hydroxypyrimidine. The mother liquor from this reaction on acid hydrolysis yields 4-hydroxy-6-methoxy-5-nitropyrimidine and reacts with MeNHNH2 to yield 4-hydroxy-6-hydrazinopyrimidine. Both 4-chloro-6-hydroxy-5-nitropyrimidine and 4,6-dichloro-5-nitropyrimidine react with MeNHNH2 in alc. to yield the corresponding methylhydrazino derivs.

IT 29939-35-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 29939-35-3 CAPLUS
CN Pyrimidine, 4,6-dimethoxy-5-nitro-2-phenyl- (CA INDEX NAME)